



UNITED STATES ENVIRONMENTAL PROTECTION AGENCY  
WASHINGTON, D.C. 20460

MAR 14 1988

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Memorandum

Subject: Inert Chemical: CGA-154281; EPA ID Number 7F3489;  
Record Number 207038; Caswell No. 298C

OFFICE OF  
PESTICIDES AND TOXIC SUBSTANCES

From: John H.S. Chen, D.V.M.  
Review Section I  
Toxicology Branch  
Hazard Evaluation Division (TS-769C)

*John H.S. Chen 3/3/88*

To: Kerry Leifer, PM 45  
Registration Support and Emergency Response Branch  
Registration Division (TS-767C)

Thru: Robert B. Jaeger, Section Head  
Review Section I  
Toxicology Branch  
Registration Division (TS-769C)

*RB 3/3/88*  
*16/11/88*  
*3/11/88*

Action Requested:

1. Review and Assessment of the Mutagenicity Studies with CGA-154281 Technical

2. Review of Registrant's Mutagenicity Overview of CGA-154281 Technical with the Assessment of Mutagenicity Studies Conducted with CGA-154281 Technical By the Ciba-Geigy's Consultant.

Petitioner: Ciba-Geigy Corp., Agricultural Division, Greensboro, NC 27419

Recommendation:

1. The Registrant should be apprised of the reporting deficiencies noted in the following studies which are identified in the detailed review:

A. Salmonella/Mammalian-Microsome Mutagenicity Test. Ciba-Geigy Limited, Experimental Pathology Laboratory Study No. 840232, June 14, 1984. Unacceptable.

B. Salmonella/Mammalian-Microsome Mutagenicity Test. Ciba-Geigy Limited, Experimental Pathology Laboratory Study No. 871077, June 30, 1987. Unacceptable.

C. Salmonella/Mammalian-Microsome Mutagenicity Test. Ciba-Geigy Limited, Experimental Pathology Laboratory Study No. 871080, June 25, 1987. Unacceptable.

(D) Autoradiographic DNA Repair Test on Rat Hepatocytes.  
Ciba-Geigy Limited, Experimental Pathology Laboratory Study No.  
850665, October 21, 1985. Unacceptable.

(E) Autoradiographic DNA Repair Test on Human Fibroblasts.  
Ciba-Geigy Limited, Experimental Pathology Laboratory Study No.  
850666. October 15, 1985. Unacceptable.

(F) Autoradiographic DNA Repair Test on Human Fibroblasts,  
Ciba-Geigy Limited, Experimental Pathology Laboratory Study No.  
860109, November 3, 1986. Unacceptable.

(G) Point Mutation Test with Chinese Hamster Cell V79.  
Ciba-Geigy Limited, Experimental Pathology Laboratory Study No.  
871160, June 29, 1987. Unacceptable.

2. The Following Mutagenicity Studies Support the Data  
Requirements for Inert Ingredients identified in the Inert Strate-  
gy document (Federal Registration/Vol. 52, No. 77, April 22, 1987,  
Pg. 13308):

A. Autoradiographic DNA Repair Test on Rat Hepatocytes,  
Ciba-Geigy Limited, Experimental Pathology Laboratory Study No.  
871076, September 17, 1987. Negative Response at 0.004-20 ug/ml.  
Acceptable.

B. Autoradiographic DNA Repair Test on Rat Hepatocytes,  
Ciba-Geigy Limited, Experimental Pathology Laboratory Study No.  
871079, July 2, 1987. Negative Response at 0.1-20 ug/ml.  
Acceptable.

C. Micronucleus Test (Chinese Hamster), Ciba-Geigy Corp.,  
Experimental Pathology Laboratory Study No. 860109, November 3,  
1986. Negative Response at 1250-5000 mg/kg. Acceptable.

3. Information was provided which demonstrates that the two  
compounds, CGA-154281 Technical and Metolachlor, are not structurally  
similar.

4. The weight of the available evidence (Study Nos. 86076  
and 860840) suggests that CGA-154281 Technical is mutagenic in  
the TA98, TA1537 and TA1538 strains of Salmonella typhimurium  
causing frameshift mutation. Further investigation of the manu-  
factured product appears necessary. They should repeat the Ames

Salmonella/Microsome Plate Assay preferably by an independent laboratory and, if necessary, remove the mutagenic impurities from the manufactured product (See detailed recommendation in our review of Registrant's mutagenicity overview of CGA-154281 Technical with the assessment of mutagenicity studies with CGA-154281 Technical by the Ciba-Geigy's consultant). Clarification is needed in order to resolve the mutagenic effects of CGA-154281 Technical in the Ames tests. Induced mutation was not demonstratable using the rat hepatocyte UDS assays (Study Nos. 860177, 871076 and 871079) and the micronucleus test (study No. 860109).

5. Toxicology Branch Recommends that the reporting deficiencies cited in our conclusion #1 and #4 must be resolved before the Agency can determine if a chronic study is needed for CGA-154281 Technical.